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VA ResearchCurrents

White House, VA conference highlights new technologies for disabled

A young quadriplegic controls a cursor on a screen solely through his thoughts. A 72-year-old woman, legally blind since her 30s, reports a new ability to make out shapes.

These were among the stunning research results shared by scientists on Oct. 13 and 14 at a Washington, DC, conference sponsored by VA and the White House Office of Science and Technology Policy. The goals of the event were to highlight advances that promise to dramatically improve the lives of Americans with disabilities, and explore ways to make the technology more accessible to consumers.

The event was titled "Emerging Technologies in Support of the New Freedom Initiative: Promoting Opportunities for People with Disabilities."

The federal New Freedom Initiative, signed into law in 2001, aims to enable those with disabilities to take better advantage of technology and to expand their access to educational, employment and social opportunities.

"In a sense, VA does for disabled veterans what the New Freedom Initiative proposes to do for all disabled Americans—remove barriers, develop new technologies, adapt environments, and do all that can be done to allow [them] the full opportunity to seek their dreams," said Pat Ryan, staff director of the Committee on Veterans Affairs of the U.S. House of Representatives and one of the speakers at the event.

The first day of the conference featured an overview of state-of-the-art technologies. John P. Donoghue, PhD, a neuroscientist at Brown University, described the "braingate system"—a tiny sensor implanted under the surface of the brain in the area that controls arm movement. The sensor picks up the electrical activity of the brain's neurons. The signals are translated into commands to control an electronic device, such as a cursor.

"We've developed computer algorithms that have helped us understand how to convert patterns of this electrical spiking activity into commands," said Donoghue, who is also an investigator with VA's new Providence-based Center for Rebuilding, Regenerating and Restoring Function After Limb Loss.

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Church-based method boosts recruitment of African American trial participants

A recent study led by a VA investigator suggests that church-based events might be an effective way to boost recruitment of older African American men into clinical research.

The study, led by Marvella E. Ford, PhD, a health-services researcher at the Michael E. DeBakey VA Medical Center and Baylor College of Medicine in Houston, compared four methods for recruiting African American men to take part in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. That trial, funded by the Centers for Disease Control and Prevention and the National Cancer Institute, is a 22-year, multisite, randomized screening trial aimed at determining whether screening for these cancers reduces mortality among older adults.

Three of the recruiting methods tested by Ford's team used special interventions targeted toward older men in Detroit's African American community—for example, a mailing featuring Dave Bing, a popular Detroit-based African American businessman and former star with the Detroit Pistons basketball team; and follow-up phone calls from African American interviewers. One of the three methods also included meetings at local churches, where prospective enrollees—the majority of whom were not members of the churches—heard a health presentation targeted toward African Americans and had their baseline information recorded.

The fourth method included only standard mail and telephone-based recruitment tactics, and was not targeted

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Recent publications and presentations

Due to space constraints, only VA authors and affiliations are noted.

"Abdominal Aortic Aneurysm: Open Versus Endovascular Repair." Frank A. Lederle, MD. **Minneapolis.** *New England Journal of Medicine,* Oct. 14, 2004.

"The Addiction Severity Index Medical and Psychiatric Composite Scores Measure Similar Domains as the SF-36 in Substance-Dependent Veterans: Concurrent and Discriminant Validity." Donald A. Calsyn, PhD; Andrew J. Saxon, MD; Kristen R. Bush, MPH; Donelle N. Howell; John S. Baer, PhD; Kevin L. Sloan, MD; Carol A. Malte, MSW; Daniel R. Kivkahan, PhD. **Puget Sound.** *Drug and Alcohol Dependence,* Nov. 11, 2004.

"Cystamine Increases L-Cysteine Levels in Huntingdon's Disease Transgenic Mouse Brain and in a PC12 Model of Polyglutamine Aggregation." Robert J. Ferrante, PhD. **Bedford.** *Journal of Neurochemistry,* Oct. 2004.

"Evidence-based Medicine Needs Medicine-based Evidence." John Concato, MD, MS, MPH. **West Haven.** Society for Epidemiologic Research annual meeting, June 2004.

"Insulin-Degrading Enzyme is Expressed in the Human Cerebrovascular Endothelium and in Cultured Human Cerebrovascular Endothelial Cells." Wenwu Gao, MD, PhD; Patricia B. Eisenhauer, PhD; Kelly Conn, PhD; John M. Wells, PhD; M. David Ullman, PhD; Ann McKee, MD; Hamant S. Thatte, PhD; Richard E. Fine, PhD. **Bedford** and **West Roxbury.** *Neuroscience Letters,* Nov. 16, 2004.

"Pattern-Match Regularity Statistic as a Measure of Characteristics of Epileptic Seizures." Deng-Shan Shiau, PhD; Wichai Suharitdamrong, MS; Sandeep P. Nair, MS; J. Chris Sackellares, MD. **Gainesville.** 34th Annual Neuroscience Meeting, Oct. 2004.

"Persistent Ascites and Low Serum Identify Patients with Cirrhosis and Low MELD Scores Who are At High Risk for Early Death." Douglas M. Heuman, MD; Souheil G. Abou-assi, MD; Adil Habib, MD; Anastasios A. Mihas, MD. **Richmond.** *Hepatology,* Oct. 2004.

"Physical Function in Sedentary and Exercising Older Veterans as Compared to National Norms." Matthew J. Peterson, MS; Gail M. Crowley, BSN, RNC; Robert J. Sullivan, MD, MPH; Miriam C. Morey, PhD. **Durham.** *Journal of Rehabilitation Research and Development,* Sept./Oct. 2004.

"Return on Educational Investment in Geriatrics Training." William B. Weeks, MD, MBA; Amy E. Wallace, MD. **White River Junction.** *Journal of the American Geriatrics Society,* Nov. 2004.

"Staphylococcus Aureus is Associated with High Bacterial Load in Chronic Wounds." Sue E. Gardner, PhD. **Iowa City.** *Wounds,* Aug. 2004.

"Thombospondin-1 Disrupts Estrogen-Induced Endothelial Cell Proliferation and Migration and its Expression is Suppressed by Estradiol." Krishanu Sengupta, PhD; Snigdha Banerjee, PhD; Neela K. Saxena, MS; Sushanta K. Banerjee, PhD. **Kansas City.** *Molecular Cancer Research,* March 2004.

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toward any specific group.

The only method that showed a statistically significant advantage was the recruitment arm that included the church-based information sessions. It yielded a 3.9 percent enrollment rate, compared to 2.9 percent for the standard recruitment arm.

"I think in Arm C [the method that used the church meetings], trust was a major component," said Ford. "I think the churches in Detroit have a lot of credibility." She added that community centers might have afforded a certain advantage, but with the churches "there was also a spiritual component."

She pointed out that the church sessions provided an opportunity to collect baseline information and signed consent forms. She said prospective participants in clinical trials often neglect to return their enrollment packets, even after they are given postage-paid envelopes and reminder phone calls. In addition, the church sessions provided face-to-face contact between potential study participants and study recruiters, which the other methods did not.

Ford said the study, published in the July 2004 issue of *Clinical Trials,* provided valuable insight into the particular obstacles involved in recruit-

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VA, Harvard study pinpoints schizophrenia brain-wave glitch

A team at the Boston VA Healthcare System and Harvard Medical School have identified a fault in the brain waves of schizophrenics that may explain their hallucinations and disturbed thinking. The study appeared in the Nov. 8 *Proceedings of the National Academy of Sciences*.

The researchers studied the brain waves of normal and schizophrenic patients as they responded to images. Those with the disorder showed no electrical activity in a certain frequency—the "gamma" range, from 30 to 100 brain waves per second—that healthy brain cells use to exchange information about the environment and form mental impressions.

"The schizophrenics did not show this gamma-band response at all. There was a pretty dramatic difference," said senior author Robert W. McCarley, MD, deputy chief of staff for mental health services and head of the Harvard psychiatry department at VA Boston Healthcare.

The brain contains hundreds of billions of neurons, or nerve cells. Researchers believe our thoughts are created when large groupings of these neurons "fire"—send messages to each other, through bursts of electrical activity—at the same frequency. Different frequencies, measured in hertz, or cycles per second, indicate different types of brain activity. Delta waves, below 4 hertz, occur during sleep. Alpha waves, 8 to 13 hertz, occur at relaxed, quiet times. Beta waves are the next fastest, occurring when we are actively thinking.

Gamma waves are harder for scientists to detect because of their low amplitude. But McCarley, lead author Kevin M. Spencer, PhD, and colleagues used a method that checks for synchronicity of the wave cycle—that is, high and low points that line up—to capture gamma activity. Successive waves "in phase" mean brain cells are communicating.

The team used electroencephalogram (EEG) to record the brain waves of 20 schizophrenic and 20 normal patients as they looked at either of two images containing "Pac-man" figures—circles with a quarter missing. In one image, the four shapes were arranged to optically suggest a square in the center. The participants had to press a button to show if they perceived the square or not.

Both groups were able to respond within a second, but those with schizophrenia made more errors and took about 200 milliseconds longer to process the images. More significantly, they showed no evidence of gamma activity "phase-locked" to the pressing of the button, which would have indicated that the brain was normally processing the visual perception guiding their response.

"What some of them did show was a response at a lower frequency, outside the gamma band, which may indicate less efficient communication among neurons," said McCarley. "If the most efficient communication between assemblies of neurons is at 40 hertz, and the schizophrenics are using a lower frequency, it's likely they have defective communication between cell assemblies and brain regions." ■

VA imaging expert to lead nationwide study of Alzheimer's disease

Michael Weiner, MD, director of the Center for Imaging of Neurodegenerative Disease at the San Francisco VA Medical Center, will lead a $60-million, five-year study to identify brain changes linked to Alzheimer's disease. The effort, funded by the National Institute on Aging and an alliance of federal, academic and private partners, will be among the largest private-public research projects ever conducted.

The study will enroll 800 older adults at up to 50 sites, including VA medical centers. Patients will undergo baseline and periodic exams including magnetic resonance imaging (MRI) or positron emission tomography, and blood, urine and spinal-cord-fluid tests. Of the participants, 200 will have a diagnosis of Alzheimer's, 200 will be cognitively normal, and 400 will have mild cognitive impairment, often a precursor to Alzheimer's.

"Those of us doing brain imaging research believe we can recognize how the brain changes in normal aging and identify specific changes related to Alzheimer's disease," said Weiner on Oct. 13 at a Washington, DC, news conference sponsored by the American Medical Association. Weiner said information gleaned from the study could lead to new therapies that stop Alzheimer's disease even before clinical symptoms appear. Currently available drugs do little more than slow the progression of the disease.

Others aims of the new trial are to standardize the

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Donoghue said neuromotor prostheses make it possible to "couple the brain to the outside world in paralyzed individuals." He showed a video of a young man with a C4 spinal cord injury, unable to move his arms or legs, who was able to move a cursor without the use of any joystick or other mechanical control.

"He is using neurosignals directly from his brain to control that cursor," explained Donoghue. "He is using his thoughts."

Among the other presenters was Joseph Rizzo, MD, an associate professor of ophthalmology at Harvard Medical School and director of the Center for Innovative Rehabilitation at the Boston VA. Rizzo described the development of a microelectronic retina implant that could potentially restore vision in cases of age-related macular degeneration or retinitis pigmentosa—both leading causes of blindness among veterans.

The system relies on a tiny digital video camera mounted in a pair of glasses. The images from the camera are sent to an ultra-thin layer of electrodes implanted in the retina. The electrodes stimulate the retina's nerve cells in a pattern resembling the video input, and the image is carried to the brain via the optic nerve.

The technology has been tested so far in six humans, including a 72-year-old blind woman who was able to distinguish cloud shapes based on input from the device. Rizzo acknowledged that substantial further research is needed before the system could have clinical applications.

"It's already taken almost two decades to get where we are. It's going to take longer to create higher-quality vision. So there's a very, very long-term horizon," said Rizzo.

Full coverage of the conference, including slide presentations and the results of breakout sessions on topics ranging from health care to transportation, will be available within the near future on the website of VA's Rehabilitation Research and Development service: www.vard.org. ■

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ing African Americans for studies. For example, African Americans may be less likely to visit a doctor regularly, and thus less likely to learn about and participate in research.

"The major difficulty with recruitment was the fact that many of the potential participants didn't appear to have a strong tie to a health care system," Ford noted. "Even though many of them are veterans, and many were former or current auto workers with health care insurance, many of them hadn't seen a doctor in years."

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brain-imaging methods used in clinical studies of Alzheimer's disease, and to develop a national database to aid scientists.

Weiner has been a VA investigator since 1980. His recently opened 10,000-square-foot center at the San Francisco VA conducts state-of-the-art imaging studies on Alzheimer's and other neurodegenerative diseases, including Gulf War Veterans' Illnesses.

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